

***The relation between science and religion is often discussed in the media — what are your views?***

For the large majority of scientists, religion has no direct impact on their research and this is not an issue that concerns them. But I don't believe that we should pretend that science and religion are 'compatible': they are actually diametrically opposed ways of thinking and acquiring knowledge. Science is revealing the incredible beauty of the world by a simple formula: the rational application of our communal common sense. In contrast, religion ultimately justifies its propositions on the basis of an individual's faith without reference to evidence, and so it is essentially anti-intellectual. Science is promulgated by our instincts to question and enquire while the different religions are promulgated by our needs for community and comforting formulas which get around death as the end of an individual's existence. Of course, science and religion can coexist (and often do in the same person), but this is more likely evidence of the agility of the human brain than, as some hopefully claim, because they deal with separate areas of understanding. The rational approach to acquiring knowledge and understanding has told us much more about what it is to be human than any religious book, and I think that all the evidence indicates that this will continue in the future.

I understand that polls of professional scientists indicate that many share broadly similar views to mine, but most shy away from publicly airing them because they don't want to be accused of being confrontational or intolerant. But the fundamental incompatibility of scientific and religious thinking is too important to skirt around and I am uncomfortable when professional scientists play along with those who try to pretend that there is no problem. Thank God for the likes of Richard Dawkins and Steve Jones, who have the patience and commitment to engage in these discussions on behalf of those of us who value rationalism and scepticism. If Dawkins didn't exist we would have to invent him.

MRC Laboratory of Molecular Biology,  
Hills Road, Cambridge CB2 2QH, UK.  
E-mail: [ll1@mrc-lmb.cam.ac.uk](mailto:ll1@mrc-lmb.cam.ac.uk)

## Obituary

### Carl R. Woese (1928–2012)

W. Ford Doolittle

Carl Woese died two days before this year began, in Urbana, Illinois, his academic home for nearly fifty years. Without the far-reaching ideas and prodigious datasets generated by Woese and his protégés, enthusiastic colleagues and hordes of more distant admirers, all of biology, but most especially microbiology and cellular evolution, would be immeasurably the poorer. Lynn Margulis, who died little more than a year before, once termed this cohort of evolutionary investigators "Woese's Army", and indeed Carl's following has that sort of character. If we sought reasons to endorse a "Great Man Theory" of (scientific) history and progress, we could find no better exemplar.

1977 was a very big year in biology, almost as important as 1953 or 1859, one might assert. Introns were discovered as 'intervening sequences' in the genes of eukaryotes, and prokaryotes were shown by Carl and his then-postdoc George Fox to be deeply divided into two groups, which Carl and George [1] called the 'urkingdoms' eubacteria and archaeobacteria.

Why were Archaea (as archaeobacteria are now called) as important as introns? First, because they drew attention to, vindicated, and ultimately led to independent tests for the whole ribocentric approach that Carl and his students had been developing over the previous decade as an objective and evolutionarily principled bacterial classification. At that time, this entailed the painstaking assembly of 'T1-catalogs' (lists of all G-terminated oligonucleotides) in 16S ribosomal (r)RNA, the molecule at the heart of all ribosome small subunits. The first catalogs took months (and intimidating amounts of  $^{32}\text{P}$  as radioactive label) to assemble. Nowadays of course complete rRNA gene sequences are obtainable many orders of magnitude more cheaply and quickly. Classification via 16S rRNA phylogeny works well at all

taxonomic levels, even down to the strain sometimes, and there are today more than 2.5 million rRNA sequences available, many being used for this purpose. 16S rRNA provides the framework within which all comparative prokaryotic physiology and genomics (three thousand genomes sequenced and counting) is currently carried out.

Second, for those who cared about evolution but not prokaryotic systematics, it was not just that the prokaryotic phylogenetic tree had a single deepest division (all bifurcating trees will), but that its two branches were so profoundly different at the molecular and cellular level. Their common ancestor must have been a primitive entity ('the progenote'), still "in the throes of evolving the genotype-phenotype coupling", Carl figured. This meant that comparative molecular biology could open a window into evolution's earliest stages, more than 3.5 billion years back. Many evolutionists, emboldened by this realization, have dedicated much of their careers to figuring out what life back then was like. Carl himself envisioned Bacteria, Archaea and Eukarya arising from an inchoate precellular community evolving through frequent gene transfer, each domain independently crossing what he called the 'Darwinian threshold'. Beyond this threshold, the increasing complexity and interconnectedness of the cellular machinery (especially ribosomes) became a barrier to information transfer: domain-specific molecular biologies emerged.

Third, for those who cared about neither systematics nor early evolution but acknowledged microbes' importance, Carl's approach would rewrite the book for microbial ecology. With the polymerase chain reaction (PCR), rRNA genes can be amplified from DNA purified straight from environmental samples. It becomes a non-problem that 90+ percent of microbes are uncultivable, at least if the goal is to know 'who is there'. By now a very clear majority of prokaryotic species, even phyla, are known to exist just because their rRNA genes have been sequenced, not because anyone has cultured them or seen them under a microscope. Initially, only environmental microbiologists



Carl Woese at the Third International Meeting on Archaeobacteria, held at Pearson College, Vancouver Island, BC, in the summer of 1988. (Photo by W.F. Doolittle.)

embraced the new methods, clinicians clinging to the pure-culture paradigm. But nowadays the first step in surveys of the microbiota of all the specialized niches in and on our own bodies (the new science now called 'microbiomics') is an RNA survey. These uses of rRNA phylogenetics we owe to the early wisdom of the army's five-star general Norman Pace, never a student of Carl's but always a staunch supporter.

And fourth, even for those in denial of the fact that this is a prokaryote-run planet, ribosomal RNA sequence comparisons would form the basis of a new appreciation for the diversity and a delineation of all the major groups of eukaryotes, this through the efforts of a friend who was a student of Woese, Mitchell Sogin. The four time-honored eukaryotic kingdoms (animals, plants, fungi and protists) are now being superseded by as many as a dozen 'supergroups', most microscopic.

Archaea had a difficult ride to acceptance. Traditionally trained microbiologists, and many systematists still embroiled in debates over whether it was molecules or morphology that could best tell us about evolution, could not countenance a radical systematic revision based on molecular sequences, partial at that. Ernst Mayr, the doyen of biological classification, did not

deny that Bacteria and Archaea are two fundamentally distinct types of prokaryotes; but he maintained that it was still the prokaryote/eukaryote divide that marked Nature's most obvious-to-carve joint. Mayr thought Woese's problem was naiveté, writing to me in 1980 that "Woese came into microbiology from outside of biology and did not (and still does not) understand what classification is all about". What was really at stake were unreconcilable understandings, not ascertainable facts. And Carl did himself no favors, with his 'urkingdoms' and 'progenotes' and heavy philosophizing, coming across as a throwback to 19<sup>th</sup> century German Romanticism. Indeed, in their different ways Woese and Mayr both engaged in 'typological thinking'.

Perhaps appropriately it was German researchers who most readily accepted the Archaea, providing the second and third legs — unique lipids and cell walls, the purview of Otto Kandler, and eukaryote-like RNA polymerases, studied by Wolfram Zillig — for the 'three-legged stool'. This last was a metaphor for the additional support that Carl's Urbana colleague Ralph Wolfe insisted would be necessary if the wider community were ever to come to believe in Archaea. Come to believe they eventually did. Today there is probably not a high-school or college textbook published that does not endorse Carl's three-domain representation of the universal Tree of Life. Admittedly, there have for the last few years been undercurrents of post-Woesian revisionism holding that: first, because of rampant lateral gene transfer persisting after cells crossed the Darwinian threshold the Tree of Life is so fuzzy as to be more properly considered a Web; second, possibly eukaryotes emerged from within the Archaea, problematizing the cladistic case for three domains; and third, Bacteria and Archaea are reified 'natural kinds'. But nobody seriously doubts that in many basic ways having to do with the mechanics of gene expression, Archaea and Bacteria are as different from each other as either is from eukaryotes. Carl did discover a third kind of Life, though one might quibble philosophically about the meaning of 'kind'.

Discovering the Archaea, or rather having the vision and fortitude

to embark, against the advice of his colleagues, on the decades-long quest for a rational microbial systematics that would result in that discovery, is far from all that biology owes to Carl Woese. Trained as a biophysicist, and in his early days pursuing rather traditional studies on mutagenesis and bacterial sporulation, he soon became fascinated with the problem of the genetic code and its origins, deciding early that the very early evolution of translation was key to understanding why cells are as they are. Presciently, he saw the ribosome as an RNA-powered molecular machine and envisioned a key role for RNA in precellular evolution, prefiguring an 'RNA world' theory that did not become widely popular until after 1977 (thanks to the discovery of introns, the other seminal event that year). And with George Fox and later Harry Noller, Carl perfected the comparative approach to determining the secondary structures of cellular RNAs: of possible secondary structures, that which is most consistent with an evolutionarily broad sampling of primary sequences is likely the true one. The method is so second-nature to us now we forget that somebody had to think it up.

Facts are facts, and Archaea would ultimately have been discovered by someone else. As scientists we cannot fully embrace Carlyle's [2] notion that "The history of what man has accomplished in this world is at the bottom the History of the Great Men who have worked here". But so much of how we think about Archaea and what they have to tell us about evolution reflects Carl's intellectual commitments that he will have left a far greater impress on the field than the rest of us could ever aspire to. He believed, even more deeply than did Dobzhansky, that "nothing makes sense in biology except in the light of evolution" and, unlike many of his colleagues trained as molecular biologists, saw mere mechanical explanations as woefully inadequate. Indeed, he declared war on molecular biology, seeing it as evolutionary biology's Scylla. The Charybdis was the Modern Synthesis, which he described as "the private domain of a quasi-scientific movement, who secreted it away in a morass of petty scholasticism" [3].

Carl was not a geneticist by training or at heart, and although cognizant of horizontal gene transfer, saw it as a creative force at the beginning of cellular evolution (the 'progenote' stage), not as a challenge to defining the 'true' relationships between living things now. Most of the phylogenetic community still holds Carl's belief as foundational. Nor was he, as Mayr complained, a card-carrying taxonomist. So he was free to invent simple intuitive treeing methods that sidestepped the cladist wars already raging at the time he started to present his startling results. Still today at big evolution meetings it is almost as if the rRNA phylogeneticists working on microbes and those who study the evolution of organisms one can see are different tribes, though some now can bridge the gap.

Carl was styled by the *Science* writer Virginia Morell [4] as "microbiology's scarred revolutionary", and the heroic story around his struggle has been told many times over, indeed now has engaged a professional historian of science as well as his colleagues. But extraordinary claims rightly demand extraordinary proofs, and Carl did in the fullness of time win many prizes — the Swedish Academy's Crafoord Prize (the real biologist's equivalent of the Nobel), a MacArthur Foundation Fellowship, the Waksman Award of the US National Academy of Sciences, the National Medal of Science, and the Leeuwenhoek Medal. And he is survived by his army, a legion of researchers owing allegiance not just to his methods but to the intellectual framework he almost singlehandedly imposed on the microbial world. None of us could hope for more.

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Department of Biochemistry and Molecular Biology, Dalhousie University, Halifax, Nova Scotia B3H 1X5, Canada.  
E-mail: [ford@dal.ca](mailto:ford@dal.ca)

## Quick guides

### Human races

Guido Barbujani<sup>1</sup>  
and Massimo Pigliucci<sup>2</sup>

**What is a race?** Ernst Mayr (1904–2005) distinguishes between species in which biological change is continuous in space, and species in which groups of populations with different character combinations are separated by borders. In the latter species, the entities separated by borders are geographic races or subspecies. Many anthropology textbooks describe human races as discrete (or nearly discrete) clusters of individuals, geographically localized, each of which shares a set of ancestors, and hence can be distinguished from other races by their common gene pool or by different alleles fixed in each.

#### *Isn't that concept elusive?*

Somewhat. Ever since Lamarck and Darwin, species are no longer regarded as fixed entities; in time, some of them split and evolve into different species. Accordingly, races are often conceptualized as populations of the same species on their way to speciation, but not quite there yet, a rather difficult category to place individuals in. Also, whether geographic variation is continuous or discontinuous may not be obvious. That said, philosophers of science recognize that concepts without sharp boundaries may still be useful in everyday as much as in scientific practice.

#### *So, maybe the concept is elusive in principle, but it works in practice?*

Yes, in some species, such as some snails or the gorilla, not to mention a number of plant species. Conversely, highly mobile species, including many birds and marine fishes, do not tend to show geographic clusters of individuals which can be distinguished morphologically or genetically.

**What about humans, then?** As you may have guessed, opinions differ among experts. Some believe not only that humans are subdivided in biological races, but also that inherited differences between races

result in a range of different abilities (including cognitive abilities). By contrast, others regard human races as entirely cultural constructs unrelated with biological diversity. There are intermediate possibilities too.

**Why then is the concept of race so widespread?** The idea that races are a natural feature of human diversity has long been the standard for anthropological research. However, scientists trying to list the human races never reached an agreement, and catalogs proposed since the 18<sup>th</sup> century contain anything between 2 and 200 races. In time, this led to questioning the meaningfulness of racial classification, so that in 1963 Frank Livingstone (1928–2005) wrote: "There are no races, there are only clines" (i.e., geographical gradients). Others disagreed. While stating that universal human rights do not derive from our being identical, but from being all humans, Theodosius Dobzhansky (1900–1975) admitted that human races are poorly defined, but maintained that they exist and predicted they would be better described in the future. The good news is that now Dobzhansky's future has arrived.

**So, what do we know now?** With a population size exceeding seven billion, humans would be expected to display a large amount of genetic variation. This is not the case, however, suggesting that population sizes were small throughout much of human history. Genetic diversity is highest in Africa and decreases as one moves away from there, probably reflecting repeated founder effects that occurred as anatomically modern humans dispersed into other continents. As a result, most human alleles have a cosmopolitan distribution, that is, they are present in all continents, at different frequencies. Combinations of alleles along the same chromosome, or haplotypes, have a clearer geographical distribution, but still only a minority of them is continent-specific. Some regions of the genome show evidence of local adaptation. Studies of ancient DNA suggest that perhaps there may have also been limited admixture with archaic humans, such as Neanderthals.